

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

*Alan Franciscus
Editor-in-Chief*

Week Ending: April 4, 2009

In This Issue:

- [VA Says 16 Colonoscopy Patients Have Hepatitis](#)
- [Synthetic blood could be in circulation within 10 years](#)
- [‘Every 15th carrier of Hepatitis C virus \(HCV\) an Indian’](#)
- [NKF 2009: Hepatitis C Virus Coinfection Accelerates Chronic Kidney Disease](#)
- [New Link In Liver Cancer](#)
- [Tattooing blamed for rise in Hep C](#)
- [International Hepatitis C Conference](#)
- [Experts say new PHARMAC funding could help avert potential public health ‘time bomb’](#)
- [Hepatitis B outbreak linked to Toms River doctor](#)
- [Pharmasset Initiates First Time in Human Study of PSI-7851 for the Treatment of Hepatitis C \(HCV\)](#)
- [Immune System's Role In Hepatitis C Recurrence After Liver Transplantation](#)
- [New Studies Examine Elimination of Hepatitis B and C](#)
- [Therapy Affected By Mutations Within A Conservative Region Of Hepatitis C Virus](#)
- [Legendary heavy-metal DJ Tawn Mastrey—the disease that took her life: Tawn's sister Cara works hard to raise awareness](#)

March 28, 2009

VA Says 16 Colonoscopy Patients Have Hepatitis

<http://www.myeyewitnessnews.com>

CHATTANOOGA, Tenn. (AP) - Veterans Affairs officials report that 16 patients exposed to contaminated equipment at its medical facilities have tested positive for viral infections, including hepatitis.

VA spokeswoman Katie Roberts said Friday that 10 colonoscopy patients from the VA medical center in Murfreesboro, Tenn., tested positive for hepatitis. She said six patients from the VA's ear, nose and throat clinic in Augusta, Ga., tested positive for unspecified viral infections.

The number of reported infections could rise. Roberts said the department doesn't yet have results from most of the more than 10,000 veterans it warned to get blood tests because they could have been exposed to contamination at those two facilities plus a medical center in Miami.

All three sites failed to properly sterilize equipment between treatments.

March 29, 2009

Synthetic blood could be in circulation within 10 years

<http://www.timesonline.co.uk>

Richard Wilson

Haemophiliac victims of contaminated transfusions remain cautiously optimistic about the research

For Bruce Norval, it is a breakthrough but one he is nevertheless wary of. He is one of more than 4,000 haemophilia sufferers who contracted Hepatitis C through contaminated blood transfusions in the 1970s and 1980s, so is cautiously optimistic about the research project conducted by Scottish scientists into the manufacture of synthetic blood from embryonic stem cells.

“It will address a lot of problems,” he says, “but we need to be able to monitor its safety and learn from the mistakes of the past.”

The three-year clinical trial, which is being led by Professor Marc Turner, the director of the Scottish National Blood Transfusion Service, — the universal blood group which can be transfused into 98% of the population without being rejected — from the stem cells. If successful, scientists believe the blood will be disease-free and provide limitless supplies for transfusions, operations and emergency procedures, reducing the reliance on donors.

By the end of the trial, they hope to be in a position to inject small amounts of the synthetic blood into volunteers to test its safety and viability, and within 10 years the process could be established on an industrial scale.

But Norval, who lives on the Black Isle, remains wary, his caution informed by his own experiences. He believes he contracted Hepatitis C when he was three years old, but the

condition remained undiagnosed until he was well into his 20s, by which time many of the symptoms were untreatable. He has now lost the feeling in his hands, suffers from night sweats and has fatty liver disease.

His chronic fatigue is so debilitating that he has to sleep in the afternoon to have enough energy to look after his children when they return home from school.

Now 44, the former nurse and welfare rights adviser had to stop working when he was 30. “My wife was five months pregnant with our first child when we found out I had Hep C,” he recalls. “I thought I’d killed them.”

He continues to campaign on behalf of fellow patients who contracted the disease through blood transfusions, and the 1,243 who were infected with HIV. Last month, it was confirmed that one haemophiliac has contracted vCJD, the human form of mad cow disease, from an infected blood donor. Which is why Norval remains guarded about the prospect of blood supplies being manufactured from stem cells.

“One thing that has been proven by haemophilia is that the current monitoring systems don’t work for prolonged side effects,” he says. “This whole synthetic blood thing is brilliant, I applaud the effort that’s going into it because of what happened to us. I’d hate for it to happen to anybody else. But I hope they’re going to ensure that the monitoring systems put in place to keep this safe are going to be as airtight as possible. Every step is exciting, but the responsibility is upon the scientists to ensure that what they’re doing isn’t ultimately going to be more harmful than what they’re trying to prevent.”

Similar research work has been carried out in America, Europe and the Far East, but the Scottish team hopes to be the first to apply what works in the laboratory to a clinical environment. Having applied to the Wellcome Trust for the £3m funding, Turner hopes that the research will begin in a matter of weeks and will build on the work which has shown that it is possible to encourage an embryonic stem cell to develop into a red blood cell.

“Even although we have a very mature and established blood service in this country, we still experience difficulties with blood shortages from time to time,” Turner says. “There are still the challenges of matching donor and patient blood, and we still have problems with transfusion-transmitted illness. When one looks at the problems that western countries face, these are of course relatively minor to the severe problems in other parts of the world. Many places just do not have a secure blood supply, or if they do, they have very high rates of infectious disease in their population.”

In the UK, 2.5m units of blood are used annually, with 80m transfused globally, but some developing countries are unable to meet their needs. Turner acknowledges the ethical and moral arguments against using embryonic stem cells in medicine, but stresses that the embryos they are using, which are three to five days old, are generated as part of routine IVF treatment and surplus to requirements, so would otherwise be discarded. He is optimistic that the study will prove successful, but he does harbour one minor objection.

“The blood is cultured rather than synthesised from scratch, it’s grown from preceding cells,” he says. “So I would describe it as cultured blood, not synthetic blood.”

'Every 15th carrier of Hepatitis C virus (HCV) an Indian'

<http://www.thaindian.com>

New Delhi, March 30 (IANS) Every 15th carrier of the Hepatitis C virus (HCV) is an Indian and 12.5 million Indians suffer from HCV, with the death rate exceeding over 100,000 per year, a doctor's conference here was told.

The most common risk factor for Hepatitis C infection today is intravenous drug use, especially through sharing of contaminated needles, the 17th annual conference of the Indian National Association for the Study of Liver (INASL) held here over the weekend was told.

In fact, 60 percent to 80 percent of all IV-drug users are infected with the HCV. Other risk factors include tattooing and body piercing if the tattoo/body piercing needles are not properly sterilized, it emerged during the conference.

According to Ajay Kumar, a senior consultant at the Indraprastha Apollo hospital here, "although hepatitis is not easily spread through sexual intercourse, high-risk behaviour, such as multiple sexual partners, is associated with an increased risk of HCV.

"Blood transfusions are another leading cause of HCV where unsuspecting patients are given blood which has the Hepatitis C virus", he added.

The conference discussed the best options for early detection, management and treatment of Hepatitis amongst various other complications affecting the liver such as acute liver failure, fatty liver disease, and hepatic encephalopathy along with recent updates on liver transplantation.

S.K. Acharya, professor and head of the Gastroenterology department at the All India Institute of Medical Sciences, said: "Hepatitis C is responsible for as many as one in four cases of liver cancer and 20 percent of chronic liver disease is because of Hepatitis C.

"However, if detected early, Hepatitis C can be cured, while Hepatitis B treatment only suppresses the infection," he added.

According to V. Saraswat of Lucknow's Sanjay Gandhi Post-Graduate Medical Institute, "there may be no symptoms in the first six months of infection. Nearly 20 percent of those infected clear the virus from their body naturally and experience no long-term effects from the infection.

"However, for the remaining 80 percent a chronic or long-term infection can develop. The course of a chronic hepatitis C infection is extremely varied and unpredictable. Because of the common absence of symptoms, many people are unaware that they have a hepatitis C infection until sometime after infection," Saraswat pointed out.

NKF 2009: Hepatitis C Virus Coinfection Accelerates Chronic Kidney Disease

www.medscape.com

Bob Roehr

March 30, 2009 (Nashville, Tennessee) — Add chronic kidney disease (CKD) to the list of diseases accelerated by hepatitis C virus (HCV) comorbidity, according to a study presented here at the National Kidney Foundation 2009 Spring Clinical Meetings.

In a retrospective analysis (from 2001 through 2004), Lama Nouredine, MD, and colleagues from Indiana University, in Bloomington, identified 111 patients with biopsy-confirmed glomerulopathy who met the additional criteria of not being on dialysis at the time of biopsy, not having experienced acute renal or hepatic failure or a transplantation, and having at least 1 follow-up creatinine level available.

"We were looking to see if patients with hepatitis C who had baseline CKD actually progressed to end-stage renal disease [ESRD]," Dr. Nouredine explained to Medscape Nephrology. "About 20% were hep C-positive [23], 60% were hep C-negative [68], and about 20% were not tested [20]" for antibodies to the virus.

They evaluated 15 covariants that could possibly affect progression to ESRD or death. The hepatitis C patients were more likely to be African American, have diabetes, and have high liver-function scores due to that coinfection. "But otherwise, there were no significant differences in any of those 15 variables, aside from the AST and the ALT" at baseline, she said.

"We found that if you were just hep C-positive (not necessarily with active or advanced disease), your odds ratio of [ESRD] or death was 4." That translated to an odds ratio of 2 for developing ESRD or death, compared with those who were negative for antibodies to HCV. "Our confidence interval did not pass 1, which is interesting for such a small number of patients," she said.

In a multivariate analysis, only HCV-positive status and age predicted death or ESRD ($P = .02$).

Looking at the change in creatinine over time, Dr. Nouredine found that those who were positive for HCV, "were at marginally statistically significant risk [$P = .08$] of having a worsening decline in creatinine. That is decent for the size of this cohort."

She pointed to other studies suggesting that the deposition of circulating immune complexes stimulated by ongoing HCV replication might lead to accelerated kidney fibrosis.

Dr. Nouredine acknowledged that a limitation of the study is that they did not have biopsy information for staging the patients' liver disease. Another issue is that industry-supported hepatitis C therapeutic trials generally exclude patients with CKD, so it is difficult to assess what, if any, effect treating 1 disease might have on progression of the other comorbidity.

In the United States, it is estimated that 1.3% to 1.9% of HCV patients aged 20 to 59 years have CKD. That rate increases to 4.3% in patients aged 40 to 49 years.

Dr. Nouredine said an earlier study by her group suggests that HCV patients who do not have

CKD at baseline are not likely to acquire the disease.

In separate study presented at the meeting, Brian Mussio, MD, and colleagues reviewed all 76 kidney biopsies performed at the Cincinnati VA Medical Center, in Ohio, during a 12-year period ending in January 2008.

They found that 18 patients (23.7%) were seropositive for HCV antibodies. Focal segmental glomerulosclerosis (FSGS) was the most commonly found pattern (5 of 18 patients) among those without diabetes. Patients with FSGS were younger (47.4 vs 53.7 years; $P = .01$), had lower serum creatinine levels at biopsy (2.0 vs 4.8 mg/dL; $P = .01$), and had a greater decline in glomerular filtration rate after biopsy (22.3 vs 2.2 mL/min/1.73m²; $P = .02$).

Both analyses were conducted without industry support. The authors have disclosed no relevant financial relationships.

National Kidney Foundation (NKF) 2009 Spring Clinical Meetings: Abstracts 218 and 217. Presented March 27, 2009.

New Link In Liver Cancer

<http://www.sciencedaily.com>

ScienceDaily (Mar. 30, 2009) — Liver damage can be triggered by various insults, including hepatitis infection or alcohol-induced cirrhosis. In severe cases, this damage can lead to cancer. A new study by researchers at the National Institutes of Health and Osaka University reveals how one protein helps decide the fate of damaged livers in mice.

Liver cells rely on signals triggered by growth hormone to survive and multiply—functions that go haywire in cancer. Normally, growth hormone works by activating a signaling network inside liver cells that includes a protein called STAT5. When the researchers removed STAT5 from liver cells, cancer ensued.

The normally protective effect of STAT5 was traced to its ability to hitch itself to a damage-inducing protein called TGFbeta and trigger its destruction. Without STAT5, TGFbeta levels soared, and growth hormone activated a related protein, STAT3, which is known to promote tumor growth.

TGFbeta and STAT5 appear to be adversaries in the liver, according to the study. STAT5 protects the liver by breaking down TGFbeta. But when TGFbeta is abundant—as occurs in people with chronic liver damage—growth hormone activates the cancer-promoting STAT3 instead of the protective STAT5. These results might help explain how chronic liver damage can eventually lead to cancer.

The study will be published online on March 30th in the *Journal of Experimental Medicine*.

Tattooing blamed for rise in Hep C

<http://www.northernstar.com.au>

Peter Weekes

YOUNG people who tattoo themselves with home kits purchased on the Internet risk contracting the potentially debilitating hepatitis C.

Two hep C experts visiting the North Coast this week yesterday told *The Northern Star* the latest surge in the number of people with the disease were young people tattooing themselves and their friends.

The kits can cost as little as \$80, but a lack of hygiene meant potential infections; those infected would pay a higher price - possibly for the rest of their lives.

Harpreet Kalsi, a trainer with the Hepatitis C Council of NSW, said there were many myths about how hep C is contracted that led to discrimination against those infected.

“It's transmitted through sharing intravenous needles, but also unsafe tattooing and piercing,” she said.

The rate of hep C infection in Australia, which is transmitted via blood, is highest on the North Coast and is the leading cause of liver transplants.

The good news is it's treatable, and between 50pc to 85pc of cases the virus can be eradicated.

“There is no vaccine for it, and the rate of infection is much higher than HIV and second only to chlamydia,” another hep C educator, Leon Fernandes, said.

Clinical nurse consultant at Lismore's Liver Clinic, Wendy Evans, said people could be infected for 20 years without knowing they were carrying the disease.

“Sometimes, when someone is young, they can have one drug experience and not think about it until much later in life when they disease starts to show itself,” she said.

Ms Evans said with the increase in health tourism, people should also be aware of lax hygiene standards in overseas hospitals.

Hep C Facts

- North Coast has the highest rate of hep C infection in Australia.
- More than 200,000 Australians have hep C, but fewer than 2pc receive treatment.
- 10,000 Australian are expected to become infected this year.
- Most young people don't know hep C is a blood-borne disease.

International Hepatitis C Conference

<http://www.imt.ie>

Gary Culliton

An international Hepatitis C Conference will be held from June 11 to 19 this year at Dublin Castle

'Hepatitis C - the Third Decade and Beyond' is a three day conference being hosted by the Consultative Council on Hepatitis C. This exciting and unique conference provides a three strand programme; Workshops include a half day programme specifically designed for GP's, Nurses and other Health Care Professionals working in the community, a 'Clinical & Research Programme' and a 'Living with Hepatitis C Programme' which includes a Meet the Experts Session.

Full Programme and Conference registration details are available on the Conference website: www.hepc2009.com

Experts say new PHARMAC funding could help avert potential public health 'time bomb'

<http://www.nzdoctor.co.nz>

Media release from Roche

Health experts believe that new access to Pegasys® (peginterferon alfa-2a (40KD)), an effective antiviral treatment for two diseases, chronic hepatitis B and C, today announced by PHARMAC, will save thousands of lives and hundreds of millions of taxpayer dollars over the next twenty years.

Together, health experts consider hepatitis B & C to be among the largest public health threats facing New Zealand in the near future.

More than 140,000 New Zealanders are estimated to be suffering from Hepatitis B & C, progressive acting viral diseases that, if left untreated can eventually lead to cirrhosis of the liver, liver failure or even liver cancer.

Associate Professor Ed Gane, Hepatologist at Auckland City Hospital, says that both hepatitis B & C were, until as recently as a decade ago, considered to be incurable.

“Up to 20 per cent of patients with chronic hepatitis C or chronic hepatitis B will progress to, and eventually die from cirrhosis of the liver, liver failure or liver cancer.”

“As a result, hepatitis B and C infections together now account for more than half of referrals for liver transplantation and more than 95% of new cases of liver cancer in New Zealand.

These two diseases represent a potential time bomb for the health system – the projected numbers of HCV-related liver cancers are projected to treble over the next 20 years and untreated hepatitis C alone could cost the health system \$400 million over the next 10-15 years.”

Clinical trials have shown that up to 52 per cent of patients with the difficult to treat genotype 1, and 84 per cent with genotypes 2 and 3 hepatitis C can be virus free following treatment with

Pegasys in combination with ribavirin. Up to one third of patients with hepatitis B can also enter lasting remission after treatment with Pegasys, where levels of the hepatitis B virus fall below detectable levels.

John Hornell, Chief Executive of the Hepatitis Foundation of New Zealand, estimates that 90,000 – 110,000 New Zealanders are suffering from chronic hepatitis B infection, and another 50,000 suffering from chronic hepatitis C infection.

However, Mr Hornell says fewer than 30,000 of these are aware of their condition and able to seek treatment.

“The best treatment outcomes are seen in those people who are diagnosed and receive treatment early. Unfortunately, the treatment rate in New Zealand is low because many people with chronic hepatitis B and C simply have not been diagnosed.”

Mr Hornell said the difficulty was that many people with chronic hepatitis B & C did not experience symptoms, or if they did, the symptoms were mild or non-specific.

“It’s important that people in the highest risk categories* get tested for hepatitis B and C when they visit their GP. The message we’re spreading is that advancements in treatment like Pegasys mean that hepatitis B and C have higher success rates than were previously achievable.”

“That is why we encourage anyone who maybe at risk of carrying either of these viruses to get the diagnostic blood test, whether or not they experience symptoms, so they can receive any necessary treatment before the liver is irreversibly impaired or before they unwittingly transmit these infectious diseases to anyone else.”

Associate Professor Gane agrees, saying testing will enable earlier diagnosis of chronic hepatitis B and C. By doing so, patients will be able to adopt precautions to avoid spreading the virus further, to adopt lifestyle modifications which may prevent the progression of their liver disease to cirrhosis and to receive treatment that may help them become virus free.

Hepatitis B outbreak linked to Toms River doctor

<http://www.app.com>

Chelsea Michels

TOMS RIVER BUREAU

TOMS RIVER — Officials for the Ocean County Health Department and the New Jersey Department of Health and Senior Services say they are investigating a situation in which five people in the township were infected with hepatitis B after receiving care at a township doctor's office.

Edward Rumen, public information officer for the county health department, said two cases of hepatitis B were confirmed in late February, when the county usually only sees about five cases a year.

Additionally, state officials had received information on three more recent cases, all in Toms

River.

An investigation was launched, finding that the cluster of patients had received care from Dr. Parvez Dara, who has offices at 214 Commons Way, Toms River and 70 Lacey Road, the Whiting section of Manchester, according to a letter sent Saturday to Dara's patients.

Rumen said the letter was sent to roughly 2,800 patients informing them of the situation and urging them to receive blood tests.

He also said unsafe infection control procedures in the office of this doctor might have been a contributing factor for the hepatitis B outbreak.

"We don't know what caused it and I don't want to speculate. The investigation is ongoing," Rumen said.

He said hepatitis B is a bloodborne disease which can affect the liver, and it can range from acute, or short-term illness, and eventually lead to chronic, or long-term illness, if untreated.

"We want everyone to get their blood work done," said Rumen. "If there are others, we can take care of them while they are in an acute state."

Robert C. Conroy, an attorney representing Dr. Dara, said he was not aware of any cases of which his client is responsible.

"I'm not aware of any evidence whatsoever about the state linking Dr. Dara to this," said Conroy, of the firm of Kern Augustine Conroy & Schoppmann in Bridgewater. "'Dr. Dara is not responsible for any cases of hepatitis B."

He speculated the infection stemmed from different locations and different types of transmission.

Pharmasset Initiates First Time in Human Study of PSI-7851 for the Treatment of Hepatitis C (HCV)

<http://finance.yahoo.com>

PRINCETON, N.J., March 31 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS - News) announced today that dosing has started in a phase 1, single ascending dose (SAD) study in healthy volunteers with **PSI-7851**, a second generation nucleotide analog polymerase inhibitor of hepatitis C virus (HCV). Pharmasset filed an Investigational New Drug Application (IND) with the Food and Drug Administration (FDA) earlier this quarter.

"This is a significant milestone for Pharmasset. PSI-7851 is a wholly owned, second generation nucleotide analog that was discovered by Pharmasset scientists" stated Dr. Michelle Berrey, Pharmasset's Chief Medical Officer. "We continue to see nucleos(t)ide inhibitors as having the potential to be the cornerstone of future HCV treatment, given their higher barrier to resistance and antiviral activity across multiple HCV genotypes, characteristics that set them apart from other HCV drug classes. We look forward to reporting the first antiviral data with PSI-7851 in the second half of 2009."

About PSI-7851

PSI-7851 is a uridine nucleoside analog currently in developed for the treatment of chronic HCV infection. PSI-7851 has demonstrated in vitro anti-HCV activity with EC(50) values of 90 +/- 60 nM, which is approximately 15- to 20-fold more potent than the active metabolite of Pharmasset's first generation nucleoside polymerase inhibitor, R7128. In vitro studies of PSI-7851 have not shown evidence of any mitochondrial or other cellular toxicities that may be associated with some nucleoside analogs. The half-life of the triphosphate in primary human hepatocytes is approximately 38 hours, which suggests the possibility for once-daily dosing. Like R7128, PSI-7851 has demonstrated in vitro activity against all of the most common HCV genotypes.

About Pharmasset

Pharmasset is a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Pharmasset's primary focus is on the development of oral therapeutics for the treatment of hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in North, Central and South America, Europe, Japan and Taiwan. Clevudine is already approved for HBV in South Korea and the Philippines. It is marketed in Korea by Bukwang Pharmaceuticals under the brand name Levovir. R7128, an oral treatment for chronic HCV infection, has completed a 4-week clinical trial in combination with Pegasys® plus Copegus® through a strategic collaboration with Roche, and is initiating a Phase 2b trial. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.

Pegasys® and Copegus® are registered trademarks of Roche.

Contact

Richard E. T. Smith, Ph.D.
VP, Investor Relations and Corporate Communications
richard.smith@pharmasset.com
Office: +1 (609) 613-4181

April 1, 2009

Immune System's Role In Hepatitis C Recurrence After Liver Transplantation

<http://www.sciencedaily.com>

ScienceDaily (Apr. 1, 2009) — A new study pinpoints certain aspects of the immune system that may play a role in the recurrence and progression of hepatitis C virus (HCV) after liver transplantation.

Hepatitis C virus (HCV), which can lead to cirrhosis and liver cancer, is the leading indication for liver transplantation in the U.S. Unfortunately, the infection almost always recurs, and in about 30 percent of cases, it causes cirrhosis in the transplanted liver within five years.

Researchers don't know exactly why some patients fare worse than others, but have been trying to understand the causes. They suspect it is related to the immunological response to HCV which involves natural killer (NK) cells and the killer cell immunoglobulin-like receptors (KIR) which recognize HLA Class I antigens.

Researchers, led by Francesca Poli of Italy, examined the role of KIR genotypes and their HLA ligands in both HCV disease recurrence and its progression after liver transplantation. They retrospectively studied 151 donor-recipient pairs for transplants that occurred between 1991 and 2001. They examined liver biopsies from the recipients that were taken at 1, 3, 5, 7 and 10 years post-transplant to determine when hepatitis recurred, the degree of fibrosis and the progression to cirrhosis.

They found that hepatitis was more likely to recur when the KIR-HLA-C ligands were mismatched between donor and recipient. Also, the presence of KIR2DL3 in the recipient correlated to progression to liver fibrosis.

“Our preliminary data indicates that KIR2DL3 positive recipients would be better assigned a matched donor for the HLA-KIR ligands in order to reduce the risk of developing severe fibrosis after liver transplantation,” the authors report.

“In summary,” they conclude, “the results presented in this study have shown that disparity for HLA-C allotypes between recipient and donor may increase the risk of recurrence of hepatic inflammation and evidence the importance of the KIR2DL3 receptor in the development of the disease.”

They suggest these factors might be considered when selecting an HCV positive liver transplant candidate, to optimize the use of the limited number of organs available.

An accompanying editorial by Lucy Golden-Mason of the University of Colorado says that the study reveals interesting associations and the results could have important implications.

“Identifying variables before liver transplantation that predict more aggressive HCV recurrence is of importance, in particular in the context of donor organ shortage,” she concurs.

“Overall,” she concludes, “the data supports the model that a genetic component contributes to natural killer cell mediated control of virus as well natural killer cell mediated hepatic injury in the setting of liver transplantation for HCV.”

Journal references:

- Espadas de Arias, Alejandro; Haworth, Simone; Belli, Luca; Burra, Patrizia; Pinzello, Giovambattista; Minola, Ernesto; Boccagni, Patrizia; Torelli, Rosanna; Scalapogna, Mario; Poli, Francesca. KIR Genotype and KIR-HLA C Ligand Compatibility Affect the Severity of HCV Recurrence Following Liver Transplantation. *Liver Transplantation*, April 2009
- Golden-Mason, Lucy. NK Cells Play Divergent Roles in Shaping the Outcome of HCV Recurrence Following Liver Transplantation. *Liver Transplantation*, April 2009

Adapted from materials provided by Wiley-Blackwell.

New Studies Examine Elimination of Hepatitis B and C

<http://www.infectioncontrolday.com/>

Two new studies in the April issue of *Hepatology* explore the ways that hepatitis B virus (HBV) and hepatitis C virus (HCV) can be cleared from patients' bodies. Both HBV and HCV are global health problems. They can lead to cirrhosis and liver cancer and they cause millions of deaths each year. Treatments to contain or cure these infections have been difficult to find. Researchers continue to explore potential therapies and the immune system response to the diseases.

The first new study sheds light on the immunological response to coinfection with HBV and HCV. Researchers led by Evangelista Sagnelli of Naples, Italy, report that for patients with chronic HCV, HBV superinfection can lead to clearance of the HCV.

They compared 29 HCV patients to 29 people, matched by age, gender and risk factors, who did not have HCV. All of the patients developed acute HBV during the same time period. The patients with HCV were more likely to have a severe course of illness, and one died of liver failure. However, nearly one-quarter (six out of 24) emerged HCV-free.

“Extensive acute hepatocellular necrosis, although life-threatening, may lead to a clearance of chronic HCV infection,” the authors report. Still, the severity of acute HBV in HCV patients raises “the concern that this clinical event could become an emerging health care problem in countries with a wide spread of both HBV and HCV infection,” they write.

“Further efforts should be made to extend the use of HBV vaccination in patients with chronic HCV infection” they also suggest.

The second study, headed by Maurizia Brunetto of Pisa, Italy, recommends interferon-based therapies as a first-line approach for patients with chronic HBV, because these have the best chance of clearing hepatitis B virus surface antigen (HBsAg). The reduction of HBsAg serum levels leading to HBsAg clearance is the hallmark of a newly achieved immune control of the infection by mean of a significant reduction of virus infected hepatocytes.

The researchers retrospectively investigated the relationship between treatment regimens and changing levels of HbsAg in 386 patients in a multinational study.

“Significantly more patients treated with peginterferon alfa-2a (21 percent) or peginterferon alfa-2a plus lamivudine (17 percent) achieved HBsAg levels under 100 IU/mL at the end of treatment compared with lamivudine (1 percent),” they report.

“HBsAg clearance represents the best possible and closest to cure outcome of antiviral therapy in patients with chronic hepatitis B, but is realistic almost exclusively among patients receiving interferon-based regimens, which are recommended as a first-line therapeutic approach,” they conclude. Interferon therapy switches the chronic active hepatitis B patient in the non-active HBV carrier who lose serum HBsAg during the years after the end of therapy. If the case occurs before the development of liver cirrhosis it endows the patient with the same life expectancy of the non-HBV infected subject.

Therapy Affected By Mutations Within A Conservative Region Of Hepatitis C Virus

<http://www.medicalnewstoday.com>

At least 200 million individuals are currently infected with hepatitis C virus (HCV) worldwide. Approximately 30%-50% of patients respond to interferon/ribavirin combination therapy. Response to interferon therapy depends mainly on viral and host genetic factors. The HCV is continually mutating which allows the virus to evade the immune system and overcome interferon treatment. The 5'untranslated region (UTR) of the viral genome is the most conserved region within the viral RNA, and its structural/thermodynamic stability is a key factor for efficient binding to host ribosomes for initiating viral polyprotein translation. It is believed that more than 100 host proteins bind to this region of the virus that is termed IRES (internal ribosome entry sequences). Specific mutations in this region would alter the structure stability of viral RNA, its protein translation efficiency and consequently its ability to replicate, and thus response to therapy. Although several mutations have been observed in different HCV genotypes, no studies have investigated mutations in IRES of HCV genotype 4a; the predominant HCV genotype in Egypt and whether such mutations correlate to therapeutic response.

A research team led by Dr. Hassan M Azzazy from Egypt addressed this issue and their study was published on March 28, 2009 in the *World Journal of Gastroenterology*.

In this study, HCV RNA was extracted from 19 chronic HCV 4a patients receiving interferon/ribavirin therapy who showed dramatic differences in their response to combination therapy after initial viral clearance. IRES domain 3 was cloned and 15 clones for each patient were sequenced. The obtained sequences were aligned with genotype 4a prototype using the ClustalW program and mutations scored. Prediction of stem-loop secondary structure and thermodynamic stability of the major quasispecies in each patient was performed using the MFOLD 3.2 program with Turner energies and selected constraints on base pairing.

Analysis of RNA secondary structure revealed that insertions in domain 3 altered Watson-Crick base pairing of stems and reduced molecular stability of RNA, which may ultimately reduce binding affinity to ribosomal proteins. Insertion mutations in domain 3 were statistically more prevalent in sustained viral response patients (SVR, n = 14) as compared to breakthrough (BT, n = 5) patients.

The results of this study suggest that the presence of single nucleotide polymorphisms (SNPs) in certain positions had direct effect on the response of HCV patients to interferon therapy. Taking into consideration the positions of these mutations, different real-time PCR or other assays can be developed for detection of the SNPs to allow the prediction of the response to interferon therapy as a step for identification of patients who are more likely to respond to therapy.

Reference:

El Awady MK, Azzazy HM, Fahmy AM, Shawky SM, Badreldin NG, Yossef SS, Omran MH, Zekri ARN, Goueli SA. Positional effect of mutations in 5'UTR of hepatitis C virus 4a on patients' response to therapy. *World J Gastroenterol* 2009; 15(12): 1480-1486
<http://www.wjgnet.com/1007-9327/15/1480.asp>

Legendary heavy-metal DJ Tawn Mastrey—the disease that took her life: Tawn's sister Cara works hard to raise awareness

<http://www.citypages.com>

By Andrea Swensson

Best known locally for her work with heavy-rock station 93X, DJ Tawn Mastrey led the kind of life that is usually reserved for fiction. After hitchhiking to California at the age of 17, she put herself through broadcasting school and landed gigs as a DJ in the Bay Area and then Los Angeles, interviewing rock stars and becoming close friends with people like Slash, Ozzy Osborne, and Sammy Hagar.

During the '80s, Mastrey was credited with popularizing then-unknown bands like Mötley Crüe and Poison, pushing hair bands and heavy rock onto the commercial airwaves. Her Wikipedia page credits her for "breaking" AC/DC and the Police single "Roxanne." Mastrey's radio shows and interviews were soon picked up for national syndication. Dubbed the "Leather Nun," she was renowned by rock lovers everywhere for being a sassy, strong woman in a field traditionally reserved for egomaniacal men.

Throughout her career as a DJ, Mastrey followed a steady upward trajectory. She moved back to her home state of Minnesota and worked as a DJ on the heavy-metal-friendly station 93X during the late '90s, then took a national gig at Sirius Satellite Radio as the host of Hair Nation. But things took a dramatic turn around the time she started working for Sirius. In the early 2000s, Mastrey began to feel sick, as if she had contracted a flu that she just couldn't shake.

"She became ill and she didn't know why," says Mastrey's younger sister Cara, seated at the dining room table in her bohemian south Minneapolis apartment, surrounded by photos of Tawn. "They did all sorts of tests, and finally it came out that she had the hepatitis C virus. She didn't even know what that was."

Cara became Tawn's main caretaker, moving back to Minneapolis from Ireland to care for her ailing sibling. As Tawn's symptoms worsened and the medical bills piled high, Cara scrambled to learn more about the disease and raise money to care for her sister.

"She called me a bitch robot because I made sure the nurses were giving her medication," Cara says, smiling bashfully. She is a beautiful woman with high cheekbones and long dark hair, and her eyes sparkle with the same mischief that lights up so many of her sister's old photographs.

Without health insurance, Tawn's options became increasingly limited. "She was not able to afford the treatment," Cara explains. "So she figured, well, I'll just live my life like most people with these diseases do." Surrounded by her family, Tawn's energy and vitality were slowly and steadily whittled away, and on October 2, 2007, the disease took her life. Tawn was 53.

"She felt personally responsible, having hepatitis C," Cara says. "She really felt it was imperative that the word needs to get out there."

Taking the lead from similar hepatitis C-awareness foundations like Donate Life America and the Greatest Gift, Cara Mastrey created a foundation that could draw on her sister's connections to the rock community to spread the word.

"People aren't getting themselves tested because they don't even know there is that disease," Cara says. "It becomes dormant in your body for up to 30 years before you feel any symptoms at all. So when you think about how you get hepatitis C, through blood transferral—through unscreened [donated] blood in the '70s and '80s, or intravenous drug use, tattoos, brushing your teeth with someone else's toothbrush...you never know how things can spread. Our foundation is to spread awareness to people, to encourage them to get tested so they can get treated."

The Tawn Mastrey Foundation was formed last year, and this Saturday's benefit show is the foundation's first official fundraising event. Cara has assembled a crew of her sister's old assistants to help her organize the event. She calls them "Tawn Mastrey's bitches."

"I'm the alpha bitch," she says, grinning.

Musicians are lining up to help. Fergie Frederiksen of Toto will perform at Saturday's show, Sammy Hagar has donated a song for a forthcoming compilation CD, and stars like Alice Cooper have donated autographed memorabilia for a silent auction.

As she moves forward with the foundation, Cara says she thinks back to her sister's final words of support. In the words of Tawn Mastrey: "Rock hard, live long."

The CELEBRATING TAWN MASTREY'S LIFE benefit show will include performances by Fergie Frederiksen, Scarlet Haze, Sunshine Behavior, and many more on SATURDAY, APRIL 4, at STATION 4. For more information visit tawnmastreyfoundation.com.